

Assessment of myometrial and cervical invasion of endometrial cancer by transvaginal sonography

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Summary

Introduction: The aim of this study was to determine the efficiency of transvaginal ultrasonography in the assessment of myometrial invasion and cervical involvement (preoperative staging) of endometrial cancer.

Materials and Methods: Transvaginal ultrasonography was performed on 52 women to classify endometrial cancer with respect to myometrial invasion and cervical involvement according to the International Federation of Gynaecologists and Obstetricians recommendations for surgical staging of endometrial cancer. Endometrial cancer was diagnosed on the basis of dilatation and curettage and the degree of invasion was evaluated preoperatively by transvaginal ultrasonography. Ultrasonographic findings were compared to the surgical staging and histopathology of the surgical specimen.

Results: Myometrial invasion evaluated by transvaginal sonography was accurate in 46 of 52 cases (accuracy 88%, sensitivity 86%, specificity 90%, positive predictive value 92%, negative predictive value 83%). Tumor extension to the cervix was properly diagnosed in seven of ten women in which it was present.

Conclusion: Transvaginal ultrasonography is a reliable method for assessing myometrial invasion and cervical involvement. This non-invasive method should be included as an important tool in the establishment of individualized treatment programs for women with endometrial cancer.

Key words: Endometrium; Endometrial cancer; Transvaginal ultrasonography; Myometrial invasion.

Introduction

In the past few years, the role of ultrasonography (USG) in the diagnosis of pathological processes of the female genital tract has had a considerably growing importance, due mainly to high resolution endovaginal transducers. Several studies have shown the existence of a close relationship between the postmenopausal endometrial thickness measured by USG and the pathological changes of the endometrium. Endometrial carcinoma occurs very rarely in the presence of a thin endometrium (a total thickness of 5 mm), even in patients with bleeding disorders. However in asymptomatic cases endometrial thickness of 8 mm may be considered the maximum thickness for minimum risk [1-5].

The endometrial-myometrial border can easily be identified by USG, and the structure of both the myometrium and the cervix is relatively easy to survey. Therefore, this method offers an attractive possibility for preoperative detection of myometrial invasion. Initial reports on transabdominal USG examinations were followed by transvaginal USG, and the method was found sufficiently sensitive and specific for preoperative staging [6-10].

Our aim in this study was to determine the accuracy of preoperative USG assessment of myometrial invasion and cervical involvement in endometrial cancer.

Patients and Methods

The diagnosis of endometrial carcinoma was histologically confirmed by D&C in every patient. Fifty-two patients were examined by transvaginal USG to determine the accuracy of

this method in assessing the depth of myometrial invasion and the presence of cervical involvement. In each case we determined whether more or less than half of the thickness of the myometrium was affected by the process. Transvaginal USG was followed by staging laparotomy and depth of myometrial invasion, and the presence of cervical involvement was evaluated histologically in all cases.

The mean age of women included in the study was 65.8 years (range: 39-86). Three of them were in premenopause and the remaining 49 were in postmenopause. The latter group reported the last menstrual period at a mean time of 18.7 years before the diagnosis (range: 1-43).

In each case the same author (I. Sz.) performed transvaginal USG immediately before surgery. An ATL Ultramark 9 (Advanced Technology Laboratories, Seattle, USA) with electronic 5 MHz vaginal transducer was used. A visual angle of 90 and a depth range of 2 to 123 mm proved suitable for obtaining two-dimensional real time imaging. The organs in the small pelvis were surveyed in both the sagittal and transverse planes. When the endometrial thickness was measured in a longitudinal section, we chose the level at which the endometrial echo had maximum extension. Measurements were done between the anterior limit of the surface and the endometrial/myometrial border. When there was liquid in the uterine cavity, its diameter, measured in the same section, was subtracted from the measured thickness. The length of the uterus was measured in the same section from the fundal serosa to the cervical opening. The endometrial thickness was related to the uterine anteroposterior diameter. When the quotient of the two diameters was less than 0.5, we considered that the tumor invasion was less than half of the myometrium (Figure 1). Otherwise, the invasion was estimated to be more than 50% (Figure 2). We assumed further tumor propagation when, parallel to the changes detected in the uterus, an adnexal mass appeared (uni- or bilaterally) with or without free intra-abdominal fluid. We

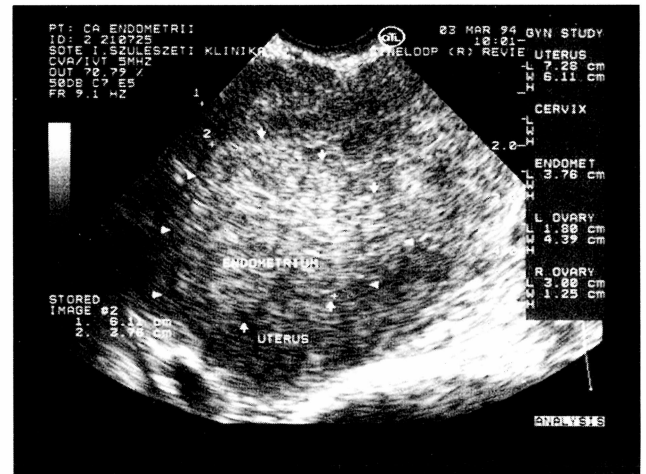


Figure 1. — Sonogram illustrating infiltration <50%. Orientation: longitudinal scan. Signs indicate the border of myometrium-endometrium. Hypoechoic endometrium thickness is 11.5 mm, anteroposterior diameter of the uterus is 45 mm. Quotient of anteroposterior diameter and endometrium is 0.25.

Figure 2. — Sonogram illustrating infiltration >50%. Orientation: longitudinal scan. Arrows indicate the border of myometrium-endometrium. Inhomogeneous endometrium thickness is 38 mm, anteroposterior diameter of the uterus is 61 mm. Quotient of anteroposterior diameter and endometrium is 0.62.

also assumed penetration of the tumor into the cervix when the cervical canal showed dilatation from the uterine cavity, or the echo of the cervical canal showed no delineation from the endometrium (Figure 3).

Surgery was performed one to four weeks after D&C. Staging and grading of the tumor were based on histological processing of the surgical specimen. Depth of myometrial invasion and the presence of cervical involvement were determined, and results were compared to those of USG assessment.

For computer analysis of the data the program package Statgraphics Version 4.0 (Statistical Graphics Corp.) was used. A difference was considered significant when using the Student's two-sample t test, p was less than 0.05.

Results

The results of our study are shown in Tables 1 and 2. As determined by transvaginal USG the endometrium was >5 mm in thickness in every case of endometrial carcinoma



Figure 3. — Sonogram of cervical infiltration. Arrows indicate the internal os of the uterus. The inhomogeneous mass of endometrium continues in the extended cervical canal.

ranging between 6.5 and 53.0 mm with a mean value of 23.5 mm. We measured more than 10 mm thickness in 88% of the patients. Its echo texture, as related to the intact myometrium, was hyperechoic in 35 cases (67.3%) and inhomogeneous in the rest of the cases. Liquid was detected in the uterine cavity on three occasions.

By transvaginal USG we reported <50% of infiltration in 24 and >50% of infiltration in 28 of the cases. Compared to the histopathological results, tumor extension was overestimated in two and underestimated in four cases (Table 3). The cervix was infiltrated by the carcinoma in ten of the 52 cases (19.2%), and that was recognized by USG in seven patients (70%).

In the present study, the preoperative staging based on transvaginal USG had a diagnostic accuracy rate of 88%. The sensitivity and specificity of this method was found at 86% and 90%, respectively.

Uterine dimensions (both longitudinal and anteroposterior) estimated by USG were significantly higher in cases with myometrial invasion >50% than in those with <50%.

The differentiation in patients with depth of myometrial invasion <50% was high (G1) in 13, moderate (G2) in seven, and low (G3) in two cases, respectively. Two patients had no data available. Twenty-three of the 28 patients with infiltration >50% had either G3 (13 cases) or G2 (10 cases) differentiation.

Discussion

Nowadays in Western countries, carcinoma of the endometrium shows an incidence as high as that of cervical cancer. Among the factors influencing the prognosis of endometrial carcinoma, histologic type, depth of myometrial invasion, presence of the cervical involvement, and tissue differentiation play a definitive role. These factors

Table 1. — Quantitative and qualitative characteristics of transvaginal ultrasonography

Qualitative characteristics	Myometrial infiltration <50%		Myometrial infiltration >50%	
Hyperechogenic endometrial tracery	18		17	
Inhomogenous endometrial tracery	6		11	
Liquid in uterine cavity	1		2	
Qualitative characteristics	Myometrial infiltration <50% (n=24)	p	Myometrial infiltration >50% (n=28)	Total (n=52)
Uterus length (mm)	63.7±10.9	p<0.05	76.6±25.5	71.2±21.5
Uterus anteroposterior diameter (mm)	45.7±9.2	p<0.05	55.8±19.8	51.6±16.9
Endometrium thickness (mm)	18.0±7.9	p<0.005	27.5±12.2	23.5±11.5
Differences of anteroposterior diameter and endometrium thickness (mm)	29.7±8.6	p<0.05	23.1±8.5	25.8±9.0
Age (year)	64.6±10.4	ns	66.7±10.5	65.8±10.4
Time following last normal period (year)	n=20 (*) 16.6±10.4	ns	n=29 (*) 19.8±9.1	n=49 (*) 18.7±9.6

(*) Patients in postmenopause; ns: not significant.

Table 2. — Comparison of tumor staging and histological tumor grading (differentiation)

Tumor stage	n.	Grade 1	Grade 2	Grade 3
I/A	8	6	2	—
I/B	14	7	5	2
I/C	19	8	4	7
II/A	3	—	—	3
II/B	1	—	—	1
III/A	6	1	3	2
IV/B	1	1	—	—

influence the incidence of metastases in both pelvic and paraaortic lymph nodes, as well as the 5-year survival rate [12, 13]. In cases with myometrial infiltration >50% metastases were found in pelvic and paraaortic lymph nodes in 46% and 18%, respectively [9]. With highly differentiated tumor and myometrial infiltration <50% without cervical involvement, the 5-year survival rate approached 100% [12, 13]. The success of oncological

Table 3. — Sensitivity of preoperative transvaginal ultrasonography in case of cancer invading >50% of myometrium (n=52)

Positive predictive value (myometrial-infiltration >50%)	26
Negative predictive value (myometrial-infiltration <50%)	20
False positive value (overestimated tumor stage, real expansion <I/C)	2
False negative value (underestimated tumor stage, real expansion >I/B)	4
Sensitivity	86%
Specificity	90%
Positive predictive value	92%
Negative predictive value	83%
Accuracy	88%

treatment requires, besides correct "grading", the preoperative prediction of the myometrial involvement with satisfactory accuracy.

Since USG is an inexpensive procedure with no side-effects, it offers a favourable method for attempting preoperative staging. The transvaginal approach has numerous advantages over the transabdominal one. The internal genital organs can be examined through the vaginal fornix from a shorter distance without being disturbed by any intermediate layer. The probe offers higher frequency and due to the increased resolution, a more detailed picture. The endometrial and the cervical structure are better defined. Although the transvaginal technique offers an unequivocally higher diagnostic efficiency, its combination with abdominal examination may supply further information in certain cases (e.g., when the uterus is extremely large) because it offers a better survey of the whole pelvis [14].

Our findings are comparable to the results obtained by others, who reported diagnostic accuracies between 78% and 92% [8-10, 15-19]. The degree of infiltration was especially difficult to determine when the uterus was large and/or deformed by myomatous foci. Cacciatore [9], Gordon [10] and Karlsson [17] reported on similar experiences. There were only two cases in our series in which the degree of myometrial invasion was overestimated. One of these was a myomatous uterus; in the other an echo texture showing no sharp delineation from the myometrium was demonstrated. In one case in which the endometrial tissue was similar to the myometrium we underestimated the degree of the myometrial invasion.

In three additional cases in which the extracorporeal extension of the tumor was underestimated by USG, histology revealed the involvement of the endocervical glands (stage II/A). In the remaining seven cases (FIGO stages II/B to III/A) preoperative ultrasonographic staging was accurate. Osmer *et al.* also underestimated stages II/A and II/B in two of 14 patients using a transducer of 5 MHz [15]. Using a 6.5 MHz probe, Artner *et al.* had three false negative cases out of nine cases with cervical infiltration; each of these belonged to FIGO stage II/A [16]. However Karlsson *et al.* had a 100% accuracy rate in diagnosing cervical extension by USG with a transducer of 7 MHz [17]. These experiences support the fact that increased accuracy in the assessment of cervical involvement can be reached by high-frequency probes.

We did not intend to study the relation of histologic grade and tumor stage. However it is noteworthy that in samples with histologically confirmed myometrial infiltration >50% we found G2 and G3 differentiation in 23 of 28 cases (82%), whereas in those with myometrial infiltration <50% only nine of the 24 patients (37.5%) had poorly differentiated tumor. Similarly to our findings Cagnazzo *et al.* reported that moderate or low tissue differentiation occurred in 57% and 47% in cases with myometrial invasion >50% and <50%, respectively [18].

In the past decade, other radiological methods have been introduced in preoperative staging of endometrial carcinoma and attempts were made to evaluate tumor markers for the same purpose [19-25]. Hysterography has failed to offer satisfactory information on tumor extension and has

carried the risk of tumor cell propagation [20]. Intrauterine USG was pushed into the background because of the same reason, though, according to Obata *et al.* the diagnostic accuracy of this method may even reach 81% [22]. Hirai *et al.* performed angiocomputerotomic examinations in 87 patients suffering from endometrial carcinoma [23]. They reached a favorable judgement when the contrast material was introduced intraarterially but intravenous introduction resulted in less favorable results. Comparative studies showed MRI as more potent than CT-scan when the extension of endometrial carcinoma was measured [24]. The endometrium appears as a sign of high intensity in the MRI pictures, thus, its extension towards the myometrium is easy to determine. When the endometrial/myometrial surface is intact, a stripe of low intensity can be identified immediately below the endometrial/myometrial border. Break up of the area of linkage can be considered myometrial invasion, regardless of the methods used [18]. The diagnostic accuracy of MRI in measuring myometrial invasion ranges between 83% and 87%. These values agree well with the efficiency of transvaginal USG [18, 25]. It should be noted, however, that MRI is an expensive and time-consuming method, thus, it is not accessible for everybody.

Among tumor markers, CA125 has been used to predict myometrial invasion. Lehtovirta *et al.* applied this method to 78 patients suffering from endometrial carcinoma [19]. The diagnostic potency of the method was compared to that of transvaginal USG. A rise in CA125 serum level meant myometrial invasion with a sensitivity of 42.8%. The rate of *positive negative prediction* was 52.9% for CA125 and 80.3% for transvaginal USG. For the latter, the following characteristics were obtained in the same study: sensitivity: 95.2%, positive predictive value: 71.4% negative predictive value: 98%, and diagnostic accuracy: 88.5%.

Our final conclusion is that transvaginal USG in spite of being difficult to perform and its restrictive use, can be applied with high diagnostic potency in preoperative staging of endometrial carcinoma. It is less extensive, simpler and more accessible than any of the other radiological diagnostic methods. It may offer information on myometrial invasion and tumor extension, and thereby help with choosing the most efficient oncological therapy for individual cases.

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